

PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:

Date of mailing (day/month/year) **See form PCT/ISA/210**

Applicant's or agent's file reference:

P1437PC00

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/EP2005/003366

International filing date (day/month/year)

24.03.2005

Priority date (day/month/year)

24.03.2004

International Patent Classification (IPC) or both national classification and IPC

C12Q1/68

Applicant

EPIGENOMICS AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/EP

Authorized officer

Facsimile No.

Telephone No.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2005/003366

Box No. 1

Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language:
_____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material
☒ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material
☒ in written format
☒ in computer readable form
 - c. time of filing/furnishing
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☒ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2005/003366

Box No. II

Priority

1. ☐ The following document has not yet been furnished:

☐ copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date in the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43bis1 and 64.1) is the claimed priority date.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/EP2005/003366

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	<u>1-22</u>	YES
	Claims	_____	NO
Inventive step (IS)	Claims	<u>1-22</u>	YES
	Claims	_____	NO
Industrial applicability (IA)	Claims	<u>1-22</u>	YES
	Claims	_____	NO

2 Citations and explanations:

1) Reference is made to the following documents:

D1: COTTRELL S E ET AL: "A real-time PCR assay for DNA-methylation using methylation-specific blockers" NUCLEIC ACIDS RESEARCH, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 32, no. 1, 13 January 2004 (2004-01-13), page e10.

D2: WO 02/070735 A (AKZO NOBEL N.V; DEIMAN, BIRGIT, ALBERTA, LOUISA, MARIA; FRANTZEN, INGE) 12 September 2002 (2002-09-12).

D3: WO 97/47762 A (SARNOFF CORPORATION) 18 December 1997 (1997-12-18).

2) Document D1 is considered the prior art closest to the subject matter of claim 1. It discloses a method of analyzing DNA methylation, comprising bisulfite conversion of the DNA, with any non-methylated cytosine bases being converted to uracil while 5-methylcytosine bases remain unchanged. Subsequent use of blocker oligonucleotides results in an increase in PCR amplification specificity.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2005/003366

Box No. V

Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement

The subject matter of the application differs from that of D1 in that the method includes a transcription-based amplification step. The subject matter of the application is therefore novel over D1 (PCT Article 33(2)).

- 3) With respect to D1, the problem addressed by the present invention can be considered that of providing an improved DNA methylation analysis. The application solves this problem by using a transcription-based amplification step in the claimed method. Documents D2 and D3 have previously disclosed methods of amplifying DNA by using a transcription-based amplification. However, none of the documents D1 to D3 includes any indication of combining the method of D1 with the transcription-based amplification according to D2 and/or D3. For this reason, the claimed subject matter of protection appears to involve an inventive step (PCT Article 33(3)).

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2005/003366

Box No. VI

Certain documents cited

1. Certain published documents (Rule 43bis.1 and 70.10)

Application No.
Patent No.

Publication date
(day/month/year)

Filing date
(day/month/year)

Priority date (valid claim)
(day/month/year)

2. Non-written disclosures (Rule 43bis.1 and 70.9)

Kind of non-written disclosure

Date of non-written disclosure
(day/month/year)

Date of written disclosure
referring to non-written disclosure
(day/month/year)

See form 210

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International application No.

PCT/EP2005/003366

Box No. I Basis of this opinion

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_____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☒

a sequence listing

☐

table(s) related to the sequence listing

b. format of material

☒

in written format

☒

in computer readable form

c. time of filing/furnishing

☐

contained in the international application as filed.

☐

filed together with the international application in computer readable form.

☒

furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2005/003366

Box No. II

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2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

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The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43bis1 and 64.1) is the claimed priority date.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/EP2005/003366

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	<u>1-22</u>	YES
	Claims	_____	NO
Inventive step (IS)	Claims	<u>1-22</u>	YES
	Claims	_____	NO
Industrial applicability (IA)	Claims	<u>1-22</u>	YES
	Claims	_____	NO

2. Citations and explanations:

1) Reference is made to the following documents:

D1: COTTRELL S E ET AL: "A real-time PCR assay for DNA-methylation using methylation-specific blockers" NUCLEIC ACIDS RESEARCH, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 32, no. 1, 13 January 2004 (2004-01-13), page e10.

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WRITTEN OPINION OF THE
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International application No.

PCT/EP2005/003366

Box No. V

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citations and explanations supporting such statement

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- 3) With respect to D1, the problem addressed by the present invention can be considered that of providing an improved DNA methylation analysis. The application solves this problem by using a transcription-based amplification step in the claimed method. Documents D2 and D3 have previously disclosed methods of amplifying DNA by using a transcription-based amplification. However, none of the documents D1 to D3 includes any indication of combining the method of D1 with the transcription-based amplification according to D2 and/or D3. For this reason, the claimed subject matter of protection appears to involve an inventive step (PCT Article 33(3)).

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International application No.

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Box No. VI

Certain documents cited

1. Certain published documents (Rule 43bis.1 and 70.10)

Application No.
Patent No.

Publication date
(day/month/year)

Filing date
(day/month/year)

Priority date (valid claim)
(day/month/year)

2. Non-written disclosures (Rule 43bis.1 and 70.9)

Kind of non-written disclosure

Date of non-written disclosure
(day/month/year)

Date of written disclosure
referring to non-written disclosure
(day/month/year)

See form 210